MISSION REPORT

Assessment of Latvia's reference microbiology laboratory system

March 2014

www.ecdc.europa.eu

ECDC MISSION REPORT

Assessment of Latvia's reference microbiology laboratory system

This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Marc J. Struelens.

Contributing authors
Polya Rosin, GrahamFraser, Marc J. Struelens

Suggested citation: European Centre for Disease Prevention and Control. Assessment of Latvia's reference microbiology laboratory system. Stockholm: ECDC; 2014.

Stockholm, August 2014

ISBN 978-92-9193-588-8

doi 10.2900/32544

Catalogue number TQ-04-14-721-EN-N

© European Centre for Disease Prevention and Control, 2014

Reproduction is authorised, provided the source is acknowledged

Contents

Figures

Tables

Abbreviations

LCDC	Latvian Centre for Disease Prevention and Control
NAC	National antimicrobial susceptibility testing committee
NHIS	National health insurance system
NRL	National reference laboratory

Executive summary

The Latvian Centre for Disease Prevention and Control – on behalf of the Ministry of Health of the Republic of Latvia – requested the European Centre for Disease Prevention and Control to evaluate the current national reference laboratory (NRL) system. The main aims were to evaluate the current structure, capabilities and activities of the NRL; and advise on options for a revision of the NRL's terms of reference and scope of services – including collaboration between laboratories and the processes of delegating NRL functions.

The evaluation took place in March 2014. Based on information shared earlier, it was apparent that Latvia has a well-organised public health system for the surveillance and control of communicable disease. The latter system is supported by reference and specialist microbiology services, based on a high level of expertise and the allocation of resources for the provision of a wide range of microbiology diagnostic services. The services provided by the officially nominated NRL covers 49 pathogens/diseases included in legislation on mandatory notification of diseases and case definitions, as well as laboratory diagnostics for a broad spectrum of others infectious diseases. All services are based on state-of-the-art technologies and are operated under quality assurance systems with ISO accreditation.

ECDC made the following main recommendations for improvements in the system:

- Legislation on NRL services should be revised to decrease the overlap in the range of tests between clinical microbiology on one side and reference testing on the other side.
- The definition of reference testing methods should be more generic and include the following reference microbiology tests that are not explicitly mentioned: microbial pathogen epidemiological typing and characterisation, confirmatory antimicrobial susceptibility testing, and determination of antimicrobial resistance determinants of public health importance.
- Latvia should consider limiting the services and functions of the NRL to services that are regularly needed (based on infectious disease statistics); other, less frequently needed services could be sub-contracted out, using a call-for-tender system.
- The implementation and monitoring of quality and biosafety standards should be promoted in all clinical and microbiology laboratories so that standards are fully adhered to.
- The collaboration between NRL and the epidemiologists at the Latvian Centre for Disease Prevention and Control (LCDC) should be improved so that joint studies could be conducted.
- Latvia should develop and implement an action plan for combatting antimicrobial resistance, establish a national antimicrobial susceptibility testing committee, nominate a national reference laboratory for antimicrobial resistance, and support the development of a national system for the surveillance of transmissible antimicrobial resistance.
- Latvia should establish cross-sector reporting on foodborne and zoonotic pathogens; results should be shared with national stakeholders to inform policy development and control measures.

Background

On behalf of the Ministry of Health of the Republic of Latvia, the Latvian Centre for Disease Prevention and Control (LCDC) contacted ECDC in September 2013 with a request for a country visit to evaluate the current national reference laboratory system. The background for this request was an ongoing review of the mandate, tasks and functions of the Latvian reference laboratories.

ECDC's mission in the area of microbiology is 'to foster the development of sufficient capacity for diagnosis, detection, identification and characterisation of infectious agents which may threaten public health'[1]. Together with the EU/EEA national microbiology focal points, an expert opinion paper was published in 2010 to define elements of best practice in the delivery of core public health support functions through national microbiology reference laboratories[2].

The terms of reference for the requested review were developed jointly by the ECDC microbiology coordination section with the national microbiology focal point and official representatives of the LCDC and the Ministry of Health of the Republic of Latvia. The ECDC visit in Riga took place from 4 to 6 March 2014.

[1] Article 5.3, Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control. Available from: http://ecdc.europa.eu/en/aboutus/Key%20Documents/0404_KD_Regulation_establishing_ECDC.pdf

[2] European Centre for Disease Prevention and Control. Core functions of microbiology reference laboratories for communicable diseases. Stockholm: ECDC; 2010. Available from: http://www.ecdc.europa.eu/en/publications/Publications/1006_TER_Core_functions_of_reference_labs.pdf

Objectives

The initial objectives of the visit were set by the Latvian Ministry of Health and the LCDC. All objectives were clarified with the ECDC team and further developed during the country visit. Objectives were:

- to review the current legal framework and structure of national reference laboratories (NRLs) for public health microbiology in Latvia and explore the role of NRLs in relation to clinical laboratory networks, healthcare, epidemiological surveillance, and preparedness;
- to review and evaluate the current capabilities and service activities of the NRLs against current national terms of reference as well as national and international reporting requirements;
- to advise on options for revision of the terms of reference defining the functions assigned to NRLs, review the list of disease-specific tests currently covered by NRL services, and clarify the scope of primary/clinical diagnostic services vs. reference microbiology testing, confirmation testing;
- to advise on priority ranking of diseases and pathogens to be included in the scope of reference microbiology services;
- to suggest processes for delegation of NRL functions, namely the criteria and procedures for assigning NRL functions, responsibilities and rights;
- to propose options for NRL collaboration with clinical microbiology laboratories, the LCDC, healthcare specialists, and international partners.

System overview

The Latvian communicable disease surveillance and control system is organised in accordance with the Epidemiological Safety Law (1997) and led by LCDC. The main functions of LCDC in the area of infectious diseases are registration, gathering and analysis of epidemiological data; investigation of cases and outbreaks; prevention and control; coordination of national immunisation programmes; issuing guidelines; consulting; education and training; and health promotion, including prevention measures. Prevention measures are handled by the Infectious Disease Risk Analysis and Prevention Department, whose regional structure is illustrated below (Figure 1).

Figure 1a. Infectious disease surveillance in Latvia: map of regional structure

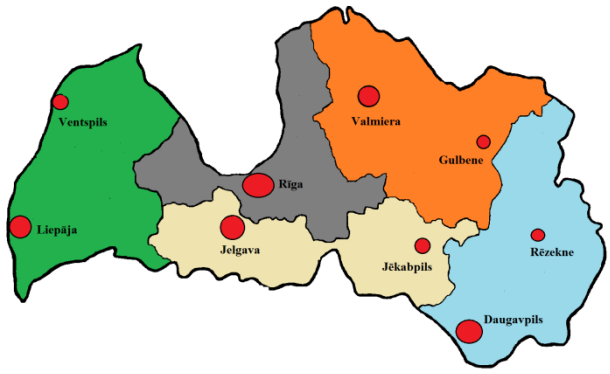


Figure 1b. Infectious disease surveillance in Latvia: number of surveillance units, population, and number of clinical microbiology laboratories

Region	Surveillance units (no)	Population (year 2013)	Clinical microbiology laboratories (2011)
Kurzeme	2	299 506	2
Latgale	2	339 783	3
Riga	1	1 060 621	8
Vidzeme	2	268 655	1
Zemgale	1	279 809	1
Total	8	2 224 400	15

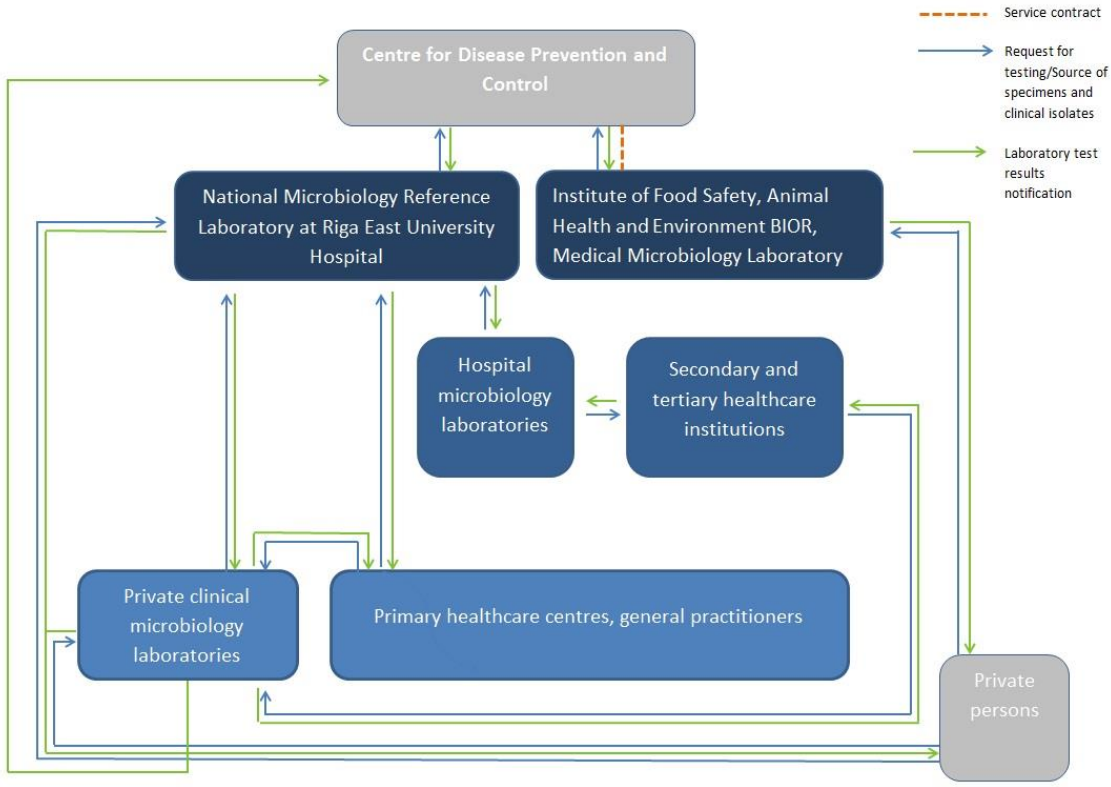
Instructions for healthcare workers and epidemiologists involved in the detection, reporting, prevention and control of communicable diseases are promulgated through ministerial level regulations, and in particular Cabinet Regulation No. 7 of 5 January 1999 on 'Procedure for registration of infectious diseases', and other regulations specific for certain infections, such as measles, rubella, poliomyelitis.

The national surveillance system is comprehensive, country wide, case based and passive. Seventy diseases and syndromes are mandatory to report[3]. Notification is done through a double reporting route, i.e. treating physicians (who have a list of 70 diseases) and public health laboratories (list of 49 diseases/pathogens) both report, using ICD 10 codes. Up-to-date EU case definitions (2012)[4] are in use and apply for reporting at the EU level. Depending on disease group, the notification process follows one of three procedures, with deadlines ranging from immediate to 72 hours, depending on the severity of the associated public health threat.

Receipt of notifiable disease reports, data entry and coding into the national surveillance system (VISUMS), follow up, including prevention and containment actions are carried out by the state epidemiologists in each region (Figure 1) as part of the LCDC responsibilities. At the national level, VISUMS offers real-time reporting and provides an interactive platform for epidemiological data queries. Routine reports are produced on a regular basis (weekly, monthly, and annual), both for internal use and for reporting to data providers and stakeholders, e.g. the Ministry of Health. These reports summarise confirmed notified cases (i.e. with laboratory diagnosis) by age, sex, and region, with limited interpretation or commentary. There are two additional computerised surveillance systems, one for HIV/AIDs, the other for tuberculosis.

Of the 70 diseases and syndromes under mandatory notification, 49 pathogens/diseases are reported by laboratories and thus include laboratory confirmation of the diagnosis. Confirmation is based on the 2012 EU case definitions. Annex 3 of Cabinet Regulation No. 7 of 5 January 1999 ('Procedure for registration of infectious diseases') provides a detailed list of these, including methods and samples to be used. Additional ministerial regulations on measles, rubella, poliomyelitis and other diseases detail laboratory diagnostics needed in case of such diseases. The figure below gives an overall, schematic representation of the laboratory services supporting communicable disease surveillance in Latvia.

Figure 2. Overview of human microbiology laboratory services in Latvia



At primary healthcare centres most cases of suspected infection are diagnosed and treated empirically. If laboratory diagnosis is sought, the specimen is obtained in the centre, or by patients presenting themselves, or the specimen, to one of the local collection points run by various networks of (mostly private) laboratories. Direct specimen transport arrangements are in place for laboratory investigation of hospitalised patients and for suspected cases of high-priority diseases. Referrals/requests for testing can be issued at the primary level to

[3] Cabinet Regulation No. 7 of 5 January 1999 'Procedure for registration of infectious diseases', annex 2

[4] Commission Implementing Decision of 8 August 2012 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32012D0506&rid=1

laboratories at the secondary/tertiary level or to laboratories which perform national reference microbiology services. Confirmatory diagnostics and/or further characterisation are required for notification of a number of pathogens/disease[5], e.g. HIV, diphtheria, etc.

Laboratory services for the 49 pathogens/diseases[6] are paid for by the national health insurance system (NHIS); patients are charged a fee for sample taking; there are no fees at specialised centres for sexually transmitted diseases. The NHIS pays for clinical microbiology services and reimburses service fees for outpatients as well as fixed fees per patient day (inpatients).

Clinical microbiology laboratories do not have to comply with specific requirements in order to have their costs reimbursed by the NHIS. Laboratories need to follow the respective national legislation for healthcare facilities and protection of workers (orders of the Cabinet of Ministers, no. 60 and no. 189). No national system exists for certifying compliance, but the above-mentioned legislation aims for ISO 151 89 accreditation by the end of 2015; according to the epidemiological safety law (1997), accreditation is mandatory for reference laboratory services.

Reference microbiology services

In Latvia, national reference microbiology services for human pathogens are provided by four laboratories:

- The National Microbiology Reference Laboratory at Riga East University Hospital was officially tasked with such services[7] in 2013, with defined core public health functions[8] and list of specialist diagnostic and reference tests.
- The Riga East University Hospital Tuberculosis and Lung Disease Centre provides reference microbiology laboratory services for *Mycobacterium tuberculosis* (neither officially nominated nor providing contract services for such work).
- The medical microbiology laboratory at the Institute of Food Safety, Animal Health and Environment (BIOR) provides reference microbiology services for selected foodborne pathogens (contracted by LCDC).
- Paul Stradinš Clinical University Hospital Microbiology Laboratory provides reference microbiology services for antimicrobial resistance testing, although it is not officially providing contract services in this area.

The core functions of the National Microbiology Reference Laboratory at Riga East University Hospital are defined in Annex 24 of Order No. 1529 of the Cabinet of Ministers:

2.1. Reference diagnostics or confirmation tests, using diagnostic algorithms, clarification of unclear cases, testing of uncommon samples.

2.2. Operation of a biological safety laboratory which can perform specific tests in situations of increased risk; provide laboratory identification of high-risk infectious disease pathogens (primary and confirmatory testing); meet International Health Regulations requirements in case of civil protection threats, disaster medicine or terrorism; detect environmental pollution with dangerous biological agents.

2.3. Provision of 24/7 preparedness and diagnostics for dangerous infectious diseases, outbreaks, epidemics and bioterrorism, including the availability of reagents to diagnose dangerous, rare and imported infections.

2.4. Monitoring, alert and response, also in collaboration with the LCDC.

2.5. Identification of imported, rare, emerging and re-emerging biological agents and maintenance of the capacity to diagnose them.

2.6. Identification of infectious diseases pathogens in accordance with case definitions as determined by legal acts of the Republic of Latvia and the European Union, including Commission Implementing Decision 2012/506/EU of 8 August 2012 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council.

2.7. Participation in working groups and infectious disease networks of the World Health Organization (WHO), the European Centre for Disease Prevention and Control (ECDC) and other international organisations in the field of public health microbiology.

[5] Cabinet Regulation No. 7 of 5 January 1999: 'Procedure for registration of infectious diseases'

[6] Annex 3 of Cabinet Regulation No. 7 of 5 January 1999: 'Procedure for registration of infectious diseases'

[7] Instruction of the Cabinet of Ministers, No. 101, 21 February 2012: 'On the establishment of the Centre for Disease Prevention and Control and the reorganisation of the governmental institutions subordinated to the Ministry of Health and the Ministry of Agriculture'. Available from: http://likumi.lv/doc.php?id=244587

[8] Annex 24 of Order No. 1529 of the Cabinet of Ministers, 17 December 2013: 'Order of healthcare organisation and financing'. Available from: http://likumi.lv/doc.php?id=263457

2.8. Methodological work, including development of proficiency tests, methodological recommendations and guidelines; technical consultations for microbiology laboratories in Latvia, healthcare workers, and LCDC staff on testing methods and procedures, and the significance and interpretation of laboratory test results.

2.9. Other duties as defined by legal acts regarding epidemiological safety.

Other important duties defined by Cabinet Regulation No. 7 'Procedure for registration of infectious diseases' are the following: confirmation of carbapenemase-producing *Enterobacteriaceae*, serotyping of *Salmonella, Shigella, Yersinia, Campylobacter, Listeria,* Shiga toxin-producing *Escherichia coli* (STEC/VTEC) and *Streptococcus pneumoniae,* identification of *Campylobacter* cultures, determination of antibiotic sensitivity of *Neisseria gonorrhoeae* if other laboratories lack this capability. The NRL performs antimicrobial susceptibility testing (*Staphylococcus aureus* [MRSA, VRSA], *Streptococcus pneumoniae* with reduced sensitivity to penicillin and others) for laboratories with limited antimicrobial susceptibility testing capacities. Annex 24 of Order No. 1529 of the Cabinet of Ministers also includes a detailed list of 200 laboratory testing methods to be performed upon request for both primary and confirmatory diagnostics, which the NRL provides for the 49 diseases/pathogens included in the national legislation on case definitions and mandatory notification. The delivery of the listed tests and reference functions are covered by NHIS through a fixed, annual budget. NRL also covers those diagnostic tests that are included in Annex 2 and Annex 16 of Order No. 1529 of the Cabinet of Ministers. The NRL organises external quality assessment schemes for 42 Latvian laboratories, which cover a range of diagnostic test including hepatitis A, B and C antibody/antigen detection, HIV antibody/antigen detection, identification of bacterial pathogens, *Corynebacterium diphtheriae* culture and toxigenicity testing. Of note, the frequency of EQA rounds appears to be less than annual per topic, and each scheme involves a variable number of laboratories per topic.

The NRL's premises cover approximately 2000 square meters, including a biosafety level 3 (BSL-3) facility[9] of about 150 square meters. Staff includes 35 specialists and 41 technicians, the equipment is up to date. The Laboratory was built with funding from the European Regional Development Fund. In 1996, the laboratory received ISO accreditation for its diagnostic and reference pathogen characterisation tests. In 2012, the NRL received accreditation in accordance with ISO 17025 and ISO 15189. It is a member of several EU and international laboratory networks organised by public health organisations (e.g. ECDC and WHO) and regularly participates in international external quality assessment schemes.

The NRL currently serves not only as a reference microbiology laboratory (funded by a fixed budget from the NHIS) but also as a clinical microbiology laboratory for the Riga East University Hospital and other medical institutions of Latvia (about 1 000 institutions). Microbiology testing for Riga East University Hospital – and some confirmatory testing work – is funded by NHIS in accordance with Annex 2 and Annex 16 of Order No. 1529 of the Cabinet of Ministers.

Reports on positive diagnostics of notifiable diseases done by the NRL are sent weekly to epidemiologists for epidemiological surveillance needs.

The laboratory at the Tuberculosis and Lung Disease Centre of Riga East University Hospital offers the following services: identification of *Mycobacterium tuberculosis* complex (primary diagnostics, culture of *M. tuberculosis*, genotyping of *M. tuberculosis* strains), confirmation of positive *M. tuberculosis* cultures, drug susceptibility testing for all *M. tuberculosis* strains, organisation of external quality assessment for *M. tuberculosis* culture and AFB microscopy, national and international training in tuberculosis laboratory diagnostics, identification of non-tuberculosis mycobacteria. The laboratory is part of the European Reference Laboratory Network for Tuberculosis (ERLN-TB) and the WHO Supranational Tuberculosis Laboratory Network (serving as Supranational Tuberculosis Reference Laboratory for Ukraine). The laboratory regularly participates in international external quality assessment schemes (via ECDC and WHO laboratory networks). Its facility is at BLS-2 level. There is no national body that assigns biosafety levels to laboratories, and this assessment as BLS-2 is based on the opinion of the laboratory head. There are plans to seek ISO 151 89 accreditation for its testing services; no other ISO accreditation is in place yet.

The Medical Microbiology Laboratory at the Institute of Food Safety, Animal Health and Environment (BIOR) provides reference microbiology services mostly for the detection and identification of *Salmonella*, *Shigella*, blood culture, and *C. diphtheriae*. It is contracted by the LCDC for epidemiological surveillance of selected foodborne pathogens (around 12% of all its clinical microbiology investigations). It also provides clinical microbiology services for regional hospitals (ca. 40% of its clinical microbiology investigations). The BIOR laboratory also delivers microbiological testing for environmental and food samples, e.g. in support of food- and waterborne outbreak investigations, as well as for animal owners and companies which manufacture, process and distribute feed and food products. It also carries out investigations of drinking water, for example the detection of *Legionella*.

[9] The country has a collaborative agreement in place with the Swedish Public Health Agency which provides diagnostic services for organisms requiring BSL-4 facilities that Latvia is lacking.

Pauls Stradinš Clinical University Hospital Microbiology Laboratory offers a wide range of reference microbiology services: antimicrobial susceptibility testing, identification of antimicrobial resistance determinants, molecular typing of antimicrobial-resistant microorganisms associated with nosocomial infections as part of national surveys and EARS-Net participation. It is a clinical microbiology laboratory, which has pioneered the implementation of EUCAST clinical breakpoints[10] in Latvia and assists other laboratories with antimicrobial susceptibility testing and molecular epidemiology of multidrug-resistant organisms. The laboratory is located in an outdated facility but has acquired modern molecular testing equipment through research grants. It is expected to move to more modern premises in the coming months. Currently, there is no ISO accreditation of services but the hospital management plans to seek ISO 15189 accreditation in the near future.

Progress and achievements

During the visit, observations and progress reports from the Ministry of Health representative indicated significant progress with regard to public health microbiology reference services, following recommendations by ECDC after earlier country visits to Latvia. The table below indicates the key elements of progress noted since 2011.

Table 1. Achievements in the field of public health microbiology after visits to Latvia by teams from the European Centre for Disease Prevention and Control (2011–2014)

Date and topic of ECDC visit	Microbiology recommendations	Steps implemented in 2014
September 2011: Surveillance and early detection and response systems in Latvia	Provide state funding of diagnostic tests for all communicable diseases under notification	In 2013, a list of 260 microbiology tests (performed by annual contract with NRL and funded by an NHIS grant) was updated.
	Diagnostic algorithms and test procedures to be developed by the national reference laboratory	Laboratory testing guidance developed (hepatitis B and C, parasitic diseases, MRSA screening, etc.) by NRL and Pauls Stradinš Clinical University Hospital
	Facilitate access to laboratory tests; provide adequate shipping options for domestic transportation of laboratory specimens	LCDC contract with BIOR network of laboratories for regional provision of testing of contacts and of environmental specimens in case of outbreaks of foodborne disease. Shipping of clinical specimens to NRL for confirmatory testing still an issue due to cost of transportation billed to patients
	Strengthen laboratory diagnostics for the surveillance of communicable diseases and improve feedback of surveillance information to stakeholders	Improved detection and reporting of pertussis and legionnaire's disease. Weekly feedback meeting between LCDC epidemiology staff and NRL microbiology staff to review surveillance and laboratory findings
September 2011: HIV, sexually transmitted infections and hepatitis B and C	Deploy point-of-care testing for HIV	Established in antenatal clinics
September 2011: Antimicrobial Resistance (AMR)	Establish National intersectoral coordination mechanism and develop National strategy/action plan on AMR	Coordination commission on AMR established at the Ministry of Health. AMR strategy in preparation
	Establish state-funded surveillance system for collecting and typing strains of healthcare-associated multidrug-resistant bacteria (MRSA, ESBL, CPE, MR-Acinetobacter)	National legislation was amended in order to establish an official monitoring system for resistant bacteria; all clinical microbiological laboratories report quarterly to EARS-Net.
September 2012: Latvia Euro-GASP expansion	Develop collaboration between Clinical Centre of Skin and STD, Riga, and NRL to increase the number of samples submitted for culture and antimicrobial susceptibility testing	Collaboration not in place. Number of *N. gonorrhoeae* isolates tested for national AMR surveillance in 2013 unchanged since 2012 (N=40)
	Amend surveillance legislation and train additional clinical laboratories for confirmation of gonococcal infection by culture and susceptibility testing	Not available. National legislation on gonococcal resistance surveillance was amended with provisions for reporting. Efforts need to be made to increase referrals from physicians for culture isolation and susceptibility testing.
	Update national diagnostic and treatment guidelines for STI	Not available

[10] As required for following EU case definitions, Commission Implementing Decision 2012/506/EU. Available from: http://www.eucast.org/clinical_breakpoints/

Date and topic of ECDC visit	Microbiology recommendations	Steps implemented in 2014
October 2012: Joint WHO–ECDC country visit to Latvia – Tuberculosis	Ensure rapid TB diagnosis by liquid culture or Xpert MTB/RIF testing for all eligible cases	Available
	Assign official national TB reference laboratory	Not done yet. The Mycobacteriology Laboratory at the Tuberculosis and Lung Disease Centre performs some microbiology reference functions for which it receives funding as NRL by NHIS. However, the laboratory has not been officially nominated as such. It currently does not have ISO accreditation and lacks an official biosafety level certification for BSL-2.
	Develop national TB laboratory development plan (as part of national TB strategy/action plan)	An action plan on the control of TB spread (2013–2015) was adopted by the Ministry of Health. It includes the nomination of a reference laboratory for TB diagnostics. The plan includes the introduction of molecular-based diagnostic systems (e.g. GeneXpert) in regional hospitals and prison hospital as well as genotyping for epidemiology purposes. The implementation of the plan needs is incomplete.
	Consider use of *M. tuberculosis* genotyping to investigate TB outbreaks and MDR-TB cases	Available.
	Training and monitoring of biosafety practices in all laboratories participating in the TB laboratory network	Risk assessments were produced; training courses for all laboratory specialists involved in high-risk procedures were held. All TB culture laboratories have biosafety equipment (BSCs, centrifuges with appropriate rotors etc.).
	NRL to organise a system for quality assurance and monitoring in all laboratories participating in the TB laboratory network	Available (bi-annual EQA rounds).

System strengths

Latvia has a well-organised public health system for communicable disease surveillance and control, supported by high-level microbiology expertise. Most importantly, it is driven by motived public health, surveillance and microbiology experts with a strong will to optimise the system and collaborate effectively with the involved stakeholders: Ministry of Health officials, LCDC staff, NRL staff, and clinical microbiologists.

The legal framework governing the contribution of microbiology laboratories to public health surveillance and communicable disease control is strong and provides reference microbiology laboratories with an extensive mandate which covers all pathogens/diseases under EU notification and beyond.

The clinical microbiology system offers an extensive range of diagnostic testing services. These are well complemented by NRL services for specialist diagnostics, confirmation/reference testing services as per national and international requirements, and cover 49 pathogens/diseases. These reference laboratory services are delivered by a highly qualified microbiology workforce and use modern technology platforms, such as these at the NRL at Riga East University Hospital. The services provided by the officially nominated NRL are based on state-of-the-art technologies operated with quality assurance systems in accordance with ISO standards. The national external quality assessment schemes organised for clinical microbiology laboratories by the NRL at Riga East University Hospital and the tuberculosis national reference laboratory provide essential support for ensuring surveillance data quality and comparability across the country.

With regard to certain high-priority diseases under EU surveillance – and based on recommendations from previous ECDC visits – significant improvements in microbiology service provision and outputs were observed (e.g. access to diagnostic testing for *Chlamydia trachomatis, Legionella pneumophila, Bordetella pertussis* and typing of *Mycobacterium tuberculosis*) as indicated in Table 1. Another important improvement is the development of a national strategy and action plan on antimicrobial resistance by the recently appointed Intersectoral Coordination Committee on Antimicrobial Resistance.

Areas for improvement and recommendations

Legislative framework

The current legislation on laboratory services to be provided by the NRL, as defined in Annex 24 of Order No. 1529 of the Cabinet of Ministers does not distinguish clearly enough between clinical microbiology and reference microbiology services. This appears to create a degree of uncertainty and confusion for healthcare practitioners and clinical laboratory managers on the scope of diagnostic service offered by clinical and reference laboratories. Most importantly, there is an overlap between state-funded diagnostic tests listed under NRL services and routine clinical tests for in- and outpatients, which leads to lack of legal clarity and the possibility to charge the costs of some diagnostic tests twice.

Recommendation: Latvia should revise the respective legislation on NRL services to decrease the overlap between clinical microbiology and reference testing. The definition of reference testing methods should be more generic and should be performed in accordance with international practice and, if available, ECDC and/or WHO guidance. Consider removing routine primary diagnostic (clinical microbiology) testing for common diseases from the terms of reference of NRLs, e.g. enteroviruses, *Salmonella* spp., etc. Clinical microbiology at NRL should be restricted to specialist techniques for the detection and identification of rare, emerging or dangerous etiologic agents.

Annex 24 (Section 2) of Order No. 1529 of the Cabinet of Ministers on reference laboratory services would benefit from a more explicit mention of pathogen characterisation and epidemiological typing services required for surveillance and outbreak investigation support. (Not type of methods and tests, but type of services; see suggested option).

Recommendation: Latvia should include epidemiological typing and pathogen characterisation in the list of reference microbiology tests, particularly molecular typing, reference/confirmatory antimicrobial susceptibility testing, and determination of antimicrobial resistance of public health importance.

Latvian legislation lists 49 disease/pathogens and several other mandatory notifiable diseases for which the reference laboratory provides services. This requires a very broad expertise and a wide range of test procedures. Some of the latter are very infrequently (or not at all) performed due to rarely occurring or non-existent indications for testing suspect cases. This is challenging for any laboratory in terms of proficiency and cost-effectiveness.

Recommendation: NRL functions could be periodically subcontracted out, using a call-for-tender system (e.g. every 3–5 years). The call should specify all NRL functions per disease or group of disease/pathogens (e.g. reference testing capabilities, diagnostic guideline development, coordination of laboratory network, support to outbreak investigations, etc.) and all requirements regarding expertise, quality standards, including necessary accreditation certificates. The LCDC and the Ministry of Health, in collaboration with a panel of external scientific experts, could evaluate NRL tenders and NRL activity reports, either annually and/or upon renewal of multiannual service contracts. Latvia should consider outsourcing diagnostic and reference services for rare/exotic diseases for which testing is available but not routinely performed in Latvia (e.g. West Nile virus); this could be done by call for tender directed at international service providers. Examples of such arrangements are available through ECDC's national microbiology focal points. This recommendation implies that there would be several laboratories providing different and complementary reference services, instead of having one NRL laboratory covering all needs.

The lack of a national system for quality and biosafety standard compliance as a formal requirement for accrediting clinical microbiology laboratories jeopardises diagnostic services and the safety of laboratory workers.

Recommendation: Latvia should develop and implement quality and biosafety standards for clinical and microbiology laboratories. The country should also create a system to check compliance with these standards as a prerequisite for licensing laboratories/reimbursing services.

Disease priorities

Antimicrobial susceptibility testing is not fully implemented and neither meets EU-EUCAST case definitions (2012) nor does it adhere to the 'EU surveillance protocol of antimicrobial resistance in foodborne pathogens' (2014). No public health funding is available for molecular surveillance and the epidemic investigation of transmissible antimicrobial resistance.

Recommendation: Latvia should develop and implement an action plan for combatting antimicrobial resistance. In addition, the country should establish a national antimicrobial susceptibility testing committee and involve clinical microbiology experts and learned/professional society leaders to liaise with EUCAST in order to promote good practice and establish standardised test for all laboratories. The ECDC team also recommended that Latvia should nominate a national reference laboratory for antimicrobial resistance, support the development of a national system for surveillance of transmissible antimicrobial resistance, provide support to outbreak investigations by providing characterisations of resistance mechanisms and strain typing, and organise external quality assessment schemes for other laboratories which perform antimicrobial susceptibility testing of human isolates. Finally, Latvia should engage in the harmonised monitoring of antimicrobial resistance of foodborne pathogens (*Salmonella* and *Campylobacter*) in accordance with the EU surveillance protocol released in 2014.

The capabilities of the Latvian reference laboratory for epidemiological typing for foodborne, hospital-acquired and drug-resistant pathogens are not fully utilised. This clearly is a missed opportunity to improve public health and food safety.

Recommendation: Latvia should enhance collaboration between NRL and LCDC epidemiologists. Public health would benefit from joint molecular epidemiological investigations at the national level. In addition, monitoring trends in the frequency and distribution of foodborne, hospital-acquired and drug-resistant pathogens would inform policy makers and support public health decisions.

Collaboration between laboratories

There appears to be no active collaboration of NRL experts with their counterparts in the veterinary and food safety sector. Joint surveillance and the reporting of zoonotic and foodborne pathogens is sorely missing.

Recommendation: Latvia should establish cross-sector reporting on foodborne and zoonotic pathogens. This could be accomplished by using NRL-BIOR laboratory data from human, animal and food samples on disease aetiology, pathogen type distribution and antimicrobial drug resistance rates. Reports should be yearly, based on joint reporting, and include a joint data analysis.

The available laboratory capacity for the diagnostics of *Campylobacter*, STEC/VTEC, *Giardia* and *Cryptosporidium* is reportedly underutilised. Reasons for this probably include the low awareness of clinicians and the lacking NHIS reimbursement for a number of tests, which could explain the very low notification rates for these diseases in Latvia in comparison with other EU countries.

Recommendation: Latvia should analyse the root causes for the low volume of diagnostic testing and reporting on *Campylobacter*, STEC/VTEC, *Giardia* and *Cryptosporidium* and explore possible ways to address this problem. The country should also develop and implement clinical and laboratory diagnostic algorithms for enteric diseases and support appropriate transportation services (courier) for the shipping of specimens to NRL facilities.

Annex 1. Terms of reference for the visit

ECDC country visit 4–6 March 2014: Assessment of Latvia's microbiology reference laboratory system

Executive summary

In September 2013 the Latvian Centre for Disease Prevention and Control contacted ECDC on behalf of the Ministry of Health of the Republic of Latvia with a request for a country visit aiming at the evaluation of the current National Reference Laboratory system. The objectives of the visit include review of the current legal framework and system organisation of National Reference Laboratories (NRLs) for public health microbiology in Latvia; evaluation of the current capabilities and service activities of the NRLs; advice on options for revision of the terms of reference defining the functions assigned to NRLs. The scope of the visit is the review of the national reference microbiology laboratories and services covering epidemic preparedness and the surveillance of communicable diseases and infection related special health issues under EU notification. The complete terms of reference for this ECDC visit to Latvia, including programme, working methods and expected outputs are outlined in this document.

Background

In September 2013 the Latvian Centre for Disease Prevention and Control contacted ECDC on behalf of the Ministry of Health of the Republic of Latvia with a request for a country visit aiming at the evaluation of the current National Reference Laboratory system. The background for this request was an on-going review at national level of the mandates, tasks and functions of the Reference Laboratories.

ECDC's mission in the area of microbiology is 'to foster the development of sufficient capacity for diagnosis, detection, identification and characterisation of infectious agents which may threaten public health'[11]. Together with the EU/EEA national microbiology focal points, a consensus expert opinion paper was published by ECDC in 2010 to define elements of best practice in the delivery of core public health support functions by National Microbiology Reference Laboratories[12].

The terms of reference of this ECDC visit, as described in this document, were developed jointly by ECDC Microbiology Coordination Section with the national microbiology focal point and official representatives of the Centre for Disease Prevention and Control and the Ministry of Health of the Republic of Latvia.

Objectives

- To review the current legal framework and system organisation of National Reference Laboratories (NRLs) for public health microbiology in Latvia and its role in the laboratory network in the country;
- To review and evaluate the current capabilities and service activities of the NRLs;
- To advise on options for revision of the terms of reference defining the functions assigned to NRLs;
- To advise on priority ranking of diseases and pathogens to be included in the scope of reference microbiology services;
- To suggest processes for delegation of NRL functions;
- To propose options for collaboration between the NRLs and other laboratories

Scope

Based on the objectives outlined above, this country visit will focus on the review of the national reference microbiology laboratories and services covering epidemic preparedness and the surveillance of communicable diseases and infection related special health issues under EU notification[13].

[11] Article 5.3, Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control. Available from: http://ecdc.europa.eu/en/aboutus/Key%20Documents/0404_KD_Regulation_establishing_ECDC.pdf

[12] European Centre for Disease Prevention and Control. Core functions of microbiology reference laboratories for communicable diseases. Stockholm: ECDC; 2010. Available from: http://www.ecdc.europa.eu/en/publications/Publications/1006_TER_Core_functions_of_reference_labs.pdf

[13] Decision No 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community; available from: http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:31998D2119&from=EN. Commission Implementing Decision of 8 August 2012 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council; available from: http://eur-

Methodology

The country visit team will apply the following methods:

- Collecting and reviewing existing information on Latvia's communicable diseases surveillance, alert, prevention and control system, including information available at ECDC from previous country visits to Latvia and information provided by the country, specifically for the objectives of the visit;
- Meeting with key national experts and stakeholders to discuss experience, current issues and plans for the NRLs;
- Visiting selected NRLs to collect more information on current operations;
- Analysing the collected information and observations made;
- Discussing preliminary conclusions and proposals with national stakeholders; and
- Further analysis and synthesis of findings, conclusions and suggestions along the objectives.

Expected deliverables

The country visit team will produce a draft report within four weeks of the visit. The draft report will be shared with the Ministry of Health and the Centre for Disease Prevention and Control of the Republic of Latvia. The country visit team will finalise the report within two weeks of receiving comments from the above-mentioned national stakeholders. The report shall outline the rationale and objectives of the visit, summarise the findings and suggested actions.

Publication of the report

Decisions in relation to publication the report rest with the Ministry of Health of the Republic of Latvia.

ECDC encourages all Member States to make ECDC country visit reports available via publishing on ECDC web pages and/or via the ECDC Advisory forum, national microbiology focal points Forum or other ECDC/Member States technical communication channels.

Confidentiality and media

Access to ECDC documents follows EU rules and, in particular, Regulation (EC) 1049/2001 and Directive (EC) 291/2006 and the relevant implementing rules concerning the obligation of transparency.

The level of confidentiality as well as dissemination of information produced or shared during the visit must be discussed and agreed by the Country (Ministry of Health) and ECDC.

Presence of the media at meetings during the visit or the organisation of a press conference is not foreseen. No media announcements, notes or press releases covering the event are expected.

lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32012D0506&rid=1. Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC; available from: http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32013D1082&qid=1407863264631&from=EN

Annex 2. Contacts

Latvia	ECDC
Dr Nicole Werner-Keišs Project manager Centre for Disease Prevention and Control Duntes iela 22 Riga, LV-1005 Latvia Phone: +371 67895816 Mobile: +371 28634899 www.spkc.gov.lv	Polya Rosin Scientific officer microbiology Microbiology Coordination Section Office of the Chief Scientist unit European Centre for Disease Prevention and Control SE-171 83 Stockholm Sweden Phone number: +46 (0)8 586 01336 Fax number: +46 (0)8 586 010 01 www.ecdc.europa.eu

Composition of the team and country counterparts

ECDC team

Marc Struelens, ECDC Chief Microbiologist and Head, Microbiology Coordination section - *team leader*;

Graham Fraser, Senior Expert Surveillance and Preparedness; and

Polya Rosin, Scientific Officer Microbiology

Latvian experts

Santa Līviņa, Head of Public Health Department, Ministry of Health

Jana Feldmane, Head of Unit, Environmental Health, Ministry of Health

Inga Šmate, Director of the LCDC

Prof. Dzintars Mozgis, LCDC, Deputy Director, Development and Epidemiological Safety

Jurijs Perevoščikovs, LCDC, Head of Department of Infectious Diseases Risk Analysis and Prevention

Dr Irina Lucenko, LCDC, Head of Unit, Infectious Diseases Surveillance and Immunisation Unit, Department of Infectious Diseases Risk Analysis and Prevention

Dr Arta Balode, Microbiologist, LCDC Public Health Analyst, Infectious Diseases Surveillance and Immunisation Unit, NMFP Alternate

Dr Nicole Werner-Keišs, LCDC, Project Manager, NMFP Member

Dr Vaira-Īrisa Kalniņa, Riga Eastern Clinical University Hospital, Head of Laboratory Services

Dr Jelena Storoženko, Riga Eastern Clinical University Hospital, Head of the National Microbiology Reference Laboratory

Svetlana Makarova, Institute of Food Safety, Animal Health and Environment BIOR, Head of the Laboratory of Medical Microbiology

Dr Didzis Gavars, E. Gulbja Laboratory

Dr Dace Rudzīte, Latvian Association of Medical Microbiologists

Dr Māris Taube, Associate professor, Director of the National Health Service

General Practitioners' Association

Annex 3. Programme

Tuesday, 4 March 2014	
14:30 – 16:00	Introductory meeting at the Ministry of Health with officials from the Ministry of Health and the Centre for Disease Prevention and Control and lead microbiologists Content: • Introduction of participants and objectives of the visit – the Ministry of Health and ECDC • Legal framework governing the current public health microbiology system; current organisation; - the Ministry of Health • Overview of new draft legislation covering NRL functions (future directions)-the Ministry of Health • Surveillance of communicable diseases - Contribution of microbiology laboratories and NRL to surveillance of communicable diseases- LCDC • Practical information on how the NRL system functions currently (tasks; services; identified challenges and need for re-organisation) – NRL Chair: the Ministry of Health Participants: representatives of the Ministry of Health, LCDC and lead microbiologists
16:00 – 16:15	Break
16:15-17:00	Discussion with all stakeholders at the Ministry of Health – what are the challenges with the current system? Chair: the Ministry of Health Participants: all stakeholders (the Ministry of Health, LCDC, NRL and other labs, microbiologists, GPs and paediatricians)
17:00	Close of day 1; ECDC team back to hotel
17:00 – 18:30	ECDC team – internal work at the hotel
19:30	Dinner
Wednesday, 5 March 2014	
8:00 – 11:00	Visit to the National Microbiology Reference Laboratory, Riga Eastern Clinical University Hospital Content: • Discussion on what the current challenges are; what is being done to address these • Observations and discussions with microbiology experts on the state-of-play Lead: Jeļena Storoženko, Riga East University Hospital, Head of National Microbiology Reference Laboratory Participants: Tatjana Kolupajeva, Head of Department – molecular biology of viral infections Natālija Zamjatina, Head of Department – virology Solvita Selderiņa, Head of Department – bacteriology Gatis Pakarna, Laboratory specialists – STD diagnostics
11:00 – 11:30	Break; change location
11:30 – 13:00	Visit to the Laboratory of the Institute of Food Safety, Animal Health and Environment BIOR Content: • Observations and discussions with microbiology experts on the state-of-play Lead: Ieva Rodze
13:00 – 14:30	Lunch; change location
14:30 – 16:00	Participants: Visit to the Laboratory of the Pauls Stradiņš Clinical University Hospital Content: • Observations and discussions with microbiology experts on the state-of-play Lead: Dr Arta Balode, microbiology laboratory Participants: Prof Edvīns Miklaševičs (AMR molecular epidemiology, Rīgas Stradiņš University)
16:00	Close of day 2; ECDC team back to hotel
16:00 – 18:00	ECDC team – internal work at hotel
18:30	Dinner

Thursday, 6 March 2014	
8:00 – 9:15	ECDC team – internal work at hotel
9:15 – 9:30	Change location
9:30 – 10:30	Follow up meeting at the Ministry of Health with microbiologists of all visited labs and LCDC experts Content: • Summary of collection information and impressions • Clarification of remaining questions • Plenary discussion Chair: LCDC Participants: NRL, microbiologists from other labs, LCDC
10:30 – 11:00	Break; ECDC team work
11:00 – 12:00	Closing meeting at the Ministry of Health with officials from the Ministry of Health and the Centre for Disease Prevention and Control Content: • Debrief by ECDC team • Preliminary conclusions and suggestions • Plenary discussion Participants: All stakeholders
12:00	Close of day 3; official end of visit
12:00 – 14:00	Lunch
14:00 – 16:30	ECDC team – internal work at the hotel
16:30	Travel to airport

Follow up

During the closing meeting it was agreed that a decision should be taken, jointly with the Ministry of Health and Centre for Disease Prevention and Control of the Republic of Latvia, on possible follow-up initiatives.